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"NO WASH" ALBUMIN-DEXTRAN DILUTION FOR DOUBLE-UNIT CORD BLOOD TRANSPLANTATION (DCBT) IS SAFE WITH APPROPRIATE MANAGEMENT AND RESULTS IN HIGH RATES OF SUSTAINED DONOR ENGRAFTMENT

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The wash of CB grafts involves additional product manipulation, risks cell loss, & delays time to infusion. We have previously reported that albumin-dextran dilution without centrifugation is feasible & safe in recipients of red blood cell (RBC) depleted DCBT > 20 kg. Concern remains, however, about the risk of severe infusion reactions. We now report our experience in 108 "no wash" DCBT recipients using RBC depleted units for the treatment of high-risk hematologic malignancies between 2/2006-8/2011. A "no wash" DCBT was planned for one additional patient who developed an anaphylaxis-type reaction 10 mls into the first unit (grade 3 severity CTCAE v4.0), infusion was aborted, & the graft was washed. This patient had similar reactions to blood products. The 108 patients transplanted with a diluted graft [median 41 years (range 6-69) & 69 kg (range 24-111)] received myeloablative (n = 80) or non-myeloablative (n = 28) conditioning, calcineurin-inhibitor/mycophenolate mofetil prophylaxis, & 4-6/6 HLA-matched grafts. Units were diluted a median of 8 fold (range 6-12) using 5:1 10% dextran 40-25% human serum albumin to a median final volume of 200 ml/unit (range 200-600). The median infused TNC x 10^7/kg was 2.7 (larger unit) & 2.0 (smaller unit) with a median post-thaw recovery of 86%. Units were infused consecutively [median 45 minutes/unit (range 15-150)] after pre-medications (acetaminophen, diphenhydramine, lorazepam). Infusion reactions & engraftment of the 108 patients transplanted with a diluted graft are shown (Table). While only 16 patients (15%) had no reactions, reactions in remaining patients were mild-moderate (10 grade 1, 36 grade 2, 46 grade 3 by CTCAE v4.0) & were easily treated. There were no grade 4-5 reactions. The most common reaction was grade 2-3 hypertension in 81 (75%) patients requiring treatment in 55 (51%) with hydralazine &/or furosemide. This was followed by nausea &/or vomiting (n = 16, 15%). The cumulative incidence of sustained donor engraftment was high: 94% for neutrophils & 85% for platelets. DCBT with albumin-dextran dilution of RBC depleted grafts is safe & effective with high rates of engraftment in patients > 20 kg. Our results are likely dependent on adequate dilution, slow infusion, & prompt infusion reaction management. Mild-moderate reactions are common but are easily treated. This approach is not recommended for patients with prior severe reactions to blood products, or for transplantation of RBC-replete units.

Table. Infusion Reactions and Engraftment After "No Wash" DCBT (n = 108)

Infusion Reactions by CTCAE v4	
No reaction	**n = 16, 15%**
Maximum severity grade 1	**n = 10, 9%**
Maximum severity grade 2	**n = 36, 33%**
Hypertension alone	29
Hypertension+other (grd 1 bradycardia or nausea/vomiting)	6
Wheezing/chest tightness	1
Maximum severity grade 3	**n = 46, 43%**
Hypertension alone	34
Hypertension+other (grd 2 chills or tachycardia; grd 1 nausea/vomiting, chest pain, hypoxia, bradycardia or fever)	12
Maximum severity grade 4-5	**n = 0, 0%**
Cumulative Incidence of Sustained Donor Engraftment	
Neutrophil engraftment by day +45	
All patients: 94% (95% CI: 90-99)	
Myeloablative: 94% (95% CI: 88-100); median 25 days (range 13-43)	
Non-myeloablative: 96% (95% CI: 88-100); median 10 days (range 7-36)	
Platelet engraftment to 20,000 by day +180	
All patients: 85% (95% CI: 78-92)	
Myeloablative: 84% (95% CI: 75-92); median 48 days (range 30-162)	
Non-myeloablative: 89% (95% CI: 77-100); median 34 days (range 9-59)	

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SUBSEQUENT HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) ASSOCIATED WITH LONGER SURVIVAL IN PATIENTS WITH RELAPSED/REFRACTORY (R/R) ACUTE MYELOGENOUS LEUKEMIA (AML) AFTER CLO+ARA-C OR ARA-C ALONE: A LANDMARK ANALYSIS FROM THE CLASSIC I TRIAL

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We previously reported the efficacy/safety outcomes of the CLASSIC I study in older patients (pts) with R/R AML (Kantarjian, EHA 2011). In this report, we evaluate the outcomes of HSCT after Clo+Ara-C or Ara-C alone in CLASSIC I.

CLASSIC I was a randomized, double-blind trial that compared Clo+Ara-C to Ara-C in pts ≥55 years with R/R AML. Pts were randomized to either Clo 40 mg/m^2 or placebo followed by Ara-C 1 g/m^2 each for 5 consecutive days. While the primary endpoint of OS did not differ between arms, there were statistically significant improvements in the secondary endpoints (ORR, CR & EFS) in the Clo+Ara-C arm. In this post-hoc analysis, patient characteristics and safety were analyzed for pts who underwent HSCT. Since the median time to HSCT was 3.8 months from the initiation of the study drug, a 4-month landmark analysis was conducted to evaluate OS following HSCT.

Among 320 pts with centrally confirmed AML (median age, 67yrs), 66 (21%; median age 63.5 yrs) underwent HSCT [Clo+Ara-C: n = 34; Ara-C: n = 32]. Of these, 47 pts (71%) went to HSCT in CR; 36 in CR from study drug [Clo+Ara-C: n = 22 vs Ara-C: n = 14] and 11 in CR from alternative therapy. 64 pts received an allogeneic transplant [sibling donor: n = 46 (70%), unrelated donor: n = 18 (27%)] and 2 (3%) were autologous transplants. Preparative regimens included myeloablative in 22 pts (33%) and reduced intensity conditioning/non-myeloablative in 43 pts (65%).

Multiple analyses were consistent with a survival benefit of HSCT: a naive estimate comparing OS in pts with and without HSCT; a 4-month landmark analysis comparing OS in pts with and without HSCT; and landmark analyses assessing the impact of HSCT on OS for patients who achieved CR. Although there was evidence that HSCT was associated with longer survival, there was little evidence of a differential effect across the treatment arms (interaction p = 0.32 [not shown]). Post HSCT safety findings were similar across treatment arms and raised no new concerns.